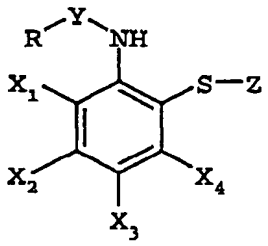
Claims

1. A CETP activity inhibitor comprising as an active ingredient a compound represented by formula (I):



(I)

wherein

R represents

a straight chain or branched C_{1-10} alkyl group;

a straight chain or branched C_{2-10} alkenyl group;

a halo-C_{1-4} lower alkyl group;

a substituted or unsubstituted C_{3-10} cycloalkyl group;

a substituted or unsubstituted C_{5-8} cycloalkenyl group;

a substituted or unsubstituted C_{3-10} cycloalkyl C_{1-10} alkyl group;

a substituted or unsubstituted aryl group;

a substituted or unsubstituted aralkyl group; or

a substituted or unsubstituted 5- or 6-membered heterocyclic group having 1-3 nitrogen, oxygen, or sulfur atoms,

X_1, X_2, X_3, and X_4 may be the same or different and represents

a hydrogen atom;

a halogen atom;

a C_{1-4} lower alkyl group;

a halo-C_{1-4} lower alkyl group;

a C_{1-4} lower alkoxy group;

a cyano group;

a nitro group;

an acyl group; or

an aryl group,

Y represents

-CO-; or

-SO_2, and

Z represents

a hydrogen atom; or
a mercapto-protecting group selected from the group consisting of
a C_{1-4} lower alkoxymethyl group,
a C_{1-4} lower alkylthiomethyl group,
an aralkyloxymethyl group having an aryl group selected from phenyl, biphenyl, and naphthyl,
an aralkylthiomethyl group having an aryl group selected from phenyl, biphenyl, and naphthyl,
a C_{3-10} cycloalkyloxymethyl group,
a C_{5-8} cycloalkenyloxymethyl group,
a C_{3-10} cycloalkyl C_{1-10} alkoxymethyl group,
an aryloxymethyl group having an aryl group selected from phenyl, biphenyl, and naphthyl,
an arylthiomethyl group having an aryl group selected from phenyl, biphenyl, and naphthyl,
an acyl group,
an acyloxy group,
an aminocarbonyloxymethyl group,
a thiocarbonyl group, and
a thio group,
provided that R is not a methyl group when Y is -CO-,
or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

2. The CETP activity inhibitor comprising as an active ingredient the compound as claimed in claim 1, wherein
R represents
a straight chain or branched C_{1-10} alkyl group;
a straight chain or branched C_{2-10} alkenyl group;
a halo-C_{1-4} lower alkyl group substituted with 1-3 halogen atoms selected from fluorine, chlorine, and bromine;
a C_{3-10} cycloalkyl group, a C_{5-8} cycloalkenyl group, or a C_{3-10} cycloalkyl C_{1-10} alkyl group, each of which may have 1-4 substituents selected from the group consisting of
a straight chain or branched C_{1-10} alkyl group,
a straight chain or branched C_{2-10} alkenyl group,

a C_{3-10} cycloalkyl group,

a C_{5-8} cycloalkenyl group,

a C_{3-10} cycloalkyl C_{1-10} alkyl group,

an aryl group selected from phenyl, biphenyl, and naphthyl,

an oxo group, and

an aralkyl group having an aryl group selected from phenyl, biphenyl, and naphthyl; or

an aryl, aralkyl, or 5- or 6-membered heterocyclic group with 1-3 nitrogen, oxygen or sulfur atoms, each of which may have 1-4 substituents selected from the group consisting of

a straight chain or branched C_{1-10} alkyl group,

a straight chain or branched C_{2-10} alkenyl group,

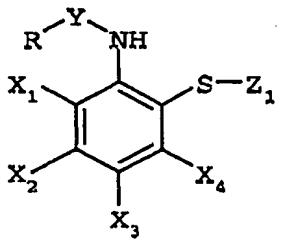
a halogen atom selected from fluorine, chlorine, and bromine,

a nitro group, and

a halo-C_{1-4} lower alkyl group having a halogen atom selected from fluorine, chlorine, and bromine;

or a prodrug compound thereof, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

3. The CETP activity inhibitor comprising as an active ingredient the compound as claimed in claim 2, which is represented by the formula (I-1):



(I-1)

wherein

R represents

a straight chain or branched C_{1-10} alkyl group;

a straight chain or branched C_{2-10} alkenyl group;

a halo-C_{1-4} lower alkyl group substituted with 1-3 halogen atoms selected from fluorine, chlorine, and bromine;

a C_{3-10} cycloalkyl group, a C_{5-8} cycloalkenyl group, or a C_{3-10} cycloalkyl

C_{1-10} alkyl group, each of which may have 1-4 substituents selected from the group consisting of

a straight chain or branched C_{1-10} alkyl group,

a straight chain or branched C_{2-10} alkenyl group,

a C_{3-10} cycloalkyl group,

a C_{5-8} cycloalkenyl group,

a C_{3-10} cycloalkyl C_{1-10} alkyl group,

an aryl group selected from phenyl, biphenyl, and naphthyl,

an oxo group, and

an aralkyl group having an aryl group selected from phenyl, biphenyl, and naphthyl; or

an aryl, aralkyl, or 5- or 6-membered heterocyclic group with 1-3 nitrogen, oxygen or sulfur atoms, each of which may have 1-4 substituents selected from the group consisting of

a straight chain or branched C_{1-10} alkyl group,

a straight chain or branched C_{2-10} alkenyl group,

a halogen atom selected from fluorine, chlorine, and bromine,

a nitro group, and

a halo-C_{1-4} lower alkyl group having a halogen atom selected from fluorine, chlorine, and bromine;

X_1, X_2, X_3, and X_4 may be the same or different and represents

a hydrogen atom;

a halogen atom;

a C_{1-4} lower alkyl group;

a halo-C_{1-4} lower alkyl group;

a C_{1-4} lower alkoxy group;

a cyano group;

a nitro group;

an acyl group; or

an aryl group,

Y represents

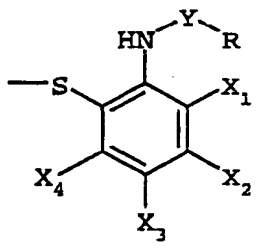
-CO-; or

$-SO_2$, and

Z_1 represents

a hydrogen atom;

a group represented by the formula



wherein R, X_1, X_2, X_3, X_4, and Y are the same as described above;

$-Y_1R_1$,

wherein Y_1 represents -CO-; or

-CS-, and

R_1 represents

a substituted or unsubstituted straight chain or branched C_{1-10} alkyl group;

a C_{1-4} lower alkoxy group;

a C_{1-4} lower alkylthio group;

a substituted or unsubstituted amino group;

a substituted or unsubstituted ureido group;

a substituted or unsubstituted C_{3-10} cycloalkyl group;

a substituted or unsubstituted C_{3-10} cycloalkyl C_{1-10} alkyl group;

a substituted or unsubstituted aryl group;

a substituted or unsubstituted aralkyl group;

a substituted or unsubstituted arylalkenyl group;

a substituted or unsubstituted arylthio group;

a substituted or unsubstituted 5- or 6-membered heterocyclic group having 1-3 nitrogen, oxygen, or sulfur atoms; or

a substituted or unsubstituted 5- or 6-membered heteroarylalkyl group; or

$-S-R_2$,

wherein R_2 represents

a substituted or unsubstituted C_{1-4} lower alkyl group; or

a substituted or unsubstituted aryl group,

or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

4. The CETP activity inhibitor comprising as an active ingredient the compound as claimed in claim 3, wherein

R_1 represents

a straight chain or branched C_{1-10} alkyl group which may have 1-3 substituents selected from the group consisting of

a halogen atom selected from fluorine, chlorine, and bromine,

a C_{1-4} lower alkoxy group,

an amino group that may be substituted with a C_{1-4} lower alkyl, acyl, or hydroxyl group,

a C_{1-4} lower alkylthio group,

a carbamoyl group,

a hydroxyl group,

an acyl group,

an acyloxy group having an acyl group,

a carboxyl group, and

an aryloxy group that may be substituted with a halogen atom selected from fluorine, chlorine, and bromine;

a C_{1-4} lower alkoxy group;

a C_{1-4} lower alkylthio group;

an amino or ureido group that may have 1-2 substituents selected from the group consisting of

a C_{1-4} lower alkyl group,

a hydroxyl group,

an acyl group, and

an aryl group that may be substituted with a lower C_{1-4} alkoxy group;

a C_{3-10} cycloalkyl or C_{3-10} cycloalkyl C_{1-10} alkyl group that may have substituents selected from the group consisting of

a straight or branched C_{1-10} alkyl group,

a C_{3-10} cycloalkyl group,

a C_{5-8} cycloalkenyl group,

an aryl group,

an amino group,

a C_{1-4} lower alkylamino group having a C_{1-4} lower alkyl group, and

an acylamino group having an acyl group;
an aryl group, an aralkyl group, an arylalkenyl group, or an arylthio group, each of which may have 1-4 substituents selected from the group consisting of
a C_{1-10} alkyl group,
a halogen atom selected from fluorine, chlorine, and bromine,
a nitro group,
a hydroxyl group,
a C_{1-4} lower alkoxy group,
a C_{1-4} lower alkylthio group,
an acyl group,
a halo-C_{1-4} lower alkyl group having a halogen atom selected from fluorine, chlorine, and bromine, and
an amino group that may be substituted with a C_{1-4} lower alkyl or acyl group;
a 5- or 6-membered heterocyclic group having 1-3 nitrogen, oxygen or sulfur atoms or a 5- or 6-membered heteroarylalkyl group that may have 1-4 substituents selected from the group consisting of
a straight chain or branched C_{1-10} alkyl group,
a halogen atom selected from fluorine, chlorine, and bromine,
an acyl group,
an oxo group, and
an halo-C_{1-4} lower alkyl group having a halogen atom selected from fluorine, chlorine, and bromine; and
R_2 represents
a C_{1-4} lower alkyl groups that may have 1-3 substituents selected from the group consisting of
a C_{1-4} lower alkoxy group,
an amino group that may be substituted with a C_{1-4} lower alkyl or acyl group,
a C_{1-4} lower alkylthio group,
a carbamoyl group,
a hydroxyl group,
a carboxyl group,
an acyl group, and
a 5- or 6-membered heterocyclic group having 1-3 nitrogen,

oxygen, or sulfur atoms; or
an aryl group that may have 1-4 substituents selected from the group consisting of
a C_{1-4} lower alkyl group,
a halogen atom selected from fluorine, chlorine, and bromine,
a nitro group,
a hydroxyl group,
a C_{1-4} lower alkoxy group,
a C_{1-4} lower alkylthio group,
an acyl group,
an amino group that may be substituted with a C_{1-4} lower alkyl or acyl group, and
a halo-C_{1-4} lower alkyl group having a halogen atom selected from fluorine, chlorine, and bromine,
or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

5. The CETP activity inhibitor comprising as an active ingredient the compound as claimed in claim 1, which is selected from the group consisting of
bis-[2-(pivaloylamino)phenyl] disulfide;
bis-[2-(2-propylpentanoylamino)phenyl] disulfide;
bis-[2-(1-methylcyclohexanecarbonylamino)phenyl] disulfide;
bis-[2-(1-isopentylcyclopentanecarbonylamino)phenyl] disulfide;
bis-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] disulfide;
N-(2-mercaptophenyl)-2,2-dimethylpropioneamide;
N-(2-mercaptophenyl)-1-isopentylcyclohexanecarboxamide;
N-(2-mercaptophenyl)-1-methylcyclohexanecarboxamide;
N-(2-mercaptophenyl)-1-isopentylcyclopentanecarboxamide;
N-(2-mercaptophenyl)-1-isopropylcyclohexanecarboxamide;
N-(4,5-dichloro-2-mercaptophenyl)-1-isopentylcyclohexane-carboxamide;
N-(4,5-dichloro-2-mercaptophenyl)-1-isopentylcyclopentane-

carboxamide;

N-(2-mercapto-5-methylphenyl)-1-isopentylcyclohexane-carboxamide;

N-(2-mercapto-4-methylphenyl)-1-isopentylcyclohexane-carboxamide;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl]thio-acetate;

S-[2-(1-methylcyclohexanecarbonylamino)phenyl] 2,2-dimethylthiopropionate;

S-[2-(pivaloylamino)phenyl]phenylthioacetate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] 2,2-dimethylthiopropionate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] 2-acetylamino-3-phenylthiopropionate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] 3-pyridinethiocarboxylate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] chloro-thioacetate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] methoxy-thioacetate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] thio-propionate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] phenoxy-thioacetate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] 2-methylthiopropionate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] 4-chlorophenoxythioacetate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] cyclo-propanethiocarboxylate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] 2-acetylamino-4-carbamoylthiobutyrate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] 2-hydroxy-2-methylthiopropionate;

S-[2-(1-isopentylcyclopentanecarbonylamino)phenyl] 2,2-dimethylthiopropionate;

S-[2-(1-isopentylcyclopentanecarbonylamino)phenyl] thio-acetate;

S-[4,5-dichloro-2-(1-isopentylcyclohexanecarbonylamino)-phenyl] 2,2-dimethylthiopropionate;

S-[4,5-dichloro-2-(1-isopentylcyclopentanecarbonylamino)-phenyl] 2,2-dimethylthiopropionate;

S-[2-(1-isopentylcyclohexanecarbonylamino)-4-trifluoro-methylphenyl] 2,2-dimethylthiopropionate;

O-methyl S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl monothiocarbonate;

S-[2-(1-methylcyclohexanecarbonylamino)phenyl]S-phenyl dithiocarbonate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] N-phenylthiocarbamate;

S-[2-(pivaloylamino)-4-trifluoromethylphenyl] 2,2-dimethylthiopropionate;

S-[4,5-dichloro-2-(1-cyclopropylcyclohexanecarbonylamino) phenyl] 2,2-dimethylthiopropionate;

S-[4,5-dichloro-2-(2-cyclohexylpropionylamino)phenyl] 2,2-dimethylthiopropionate;

S-[4,5-dichloro-2-(1-pentylcyclohexanecarbonylamino)-phenyl] 2,2-dimethylthiopropionate;

S-[4,5-dichloro-2-(1-cyclopropylmethylcyclohexane carbonylamino)phenyl] 2,2-dimethylthiopropionate;

S-[4,5-dichloro-2-(1-cyclohexylmethylcyclohexanecarbonyl-amino)phenyl] 2,2-dimethylthiopropionate;

S-[4,5-dichloro-2-(1-isopropylcyclohexanecarbonylamino)-phenyl] 2,2-dimethylthiopropionate;

S-[4,5-dichloro-2-(1-isopentylcycloheptanecarbonylamino)-phenyl] 2,2-dimethylthiopropionate;

S-[4,5-dichloro-2-(1-isopentylcyclobutanecarbonylamino)-phenyl] 2,2-dimethylthiopropionate;

S-[2-(1-isopentylcyclohexanecarbonylamino)-4-nitrophenyl] 2,2-dimethylthiopropionate;

S-[4-cyano-2-(1-isopentylcyclohexanecarbonylamino)phenyl] 2,2-dimethylthiopropionate;

S-[4-chloro-2-(1-isopentylcyclohexanecarbonylamino)phenyl] 2,2-dimethylthiopropionate;

S-[5-chloro-2-(1-isopentylcyclohexanecarbonylamino)phenyl] 2,2-dimethylthiopropionate;

S-[4-fluoro-2-(1-isopentylcyclohexanecarbonylamino)phenyl] 2,2-dimethylthiopropionate;

S-[4,5-difluoro-2-(1-isopentylcyclohexanecarbonylamino)-phenyl] 2,2-dimethylthiopropionate;

S-[5-fluoro-2-(1-isopentylcyclohexanecarbonylamino)phenyl] 2,2-dimethylthiopropionate;

bis-[4,5-dichloro-2-(1-isopentylcyclohexanecarbonylamino)-phenyl] disulfide;

2-tetrahydrofurylmethyl 2-(1-isopentylcyclohexanecarbonyl amino)phenyl disulfide;

N-(2-mercaptophenyl)-1-ethylcyclohexanecarboxamide;

N-(2-mercaptophenyl)-1-propylcyclohexanecarboxamide;

N-(2-mercaptophenyl)-1-butylcyclohexanecarboxamide;

N-(2-mercaptophenyl)-1-isobutylcyclohexanecarboxamide;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] cyclo-hexanethiocarboxylate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] thio-benzoate;

S-[2-(1-isopentylcyclohexanecarbonylamino)phenyl] 5-carboxythiopentanoate;

S-[2-(1-isopentylcyclohexanecarbonylamino)-4-methylphenyl] thioacetate;

bis-[2-[1-(2-ethylbutyl)cyclohexanecarbonylamino]phenyl] disulfide;

N-(2-mercaptophenyl)-1-(2-ethylbutyl)cyclohexane-carboxamide;

S-[2-[1-(2-ethylbutyl)cyclohexanecarbonylamino]phenyl] 2-methylthiopropionate;

S-[2-(1-isobutylcyclohexanecarbonylamino)phenyl] 2-methyl-thiopropionate;

S-[2-[1-(2-ethylbutyl)cyclohexanecarbonylamino]phenyl] 1-acetylpiperidine-4-thiocarboxylate;

S-[2-[1-(2-ethylbutyl)cyclohexanecarbonylamino]phenyl] thioacetate;

S-[2-[1-(2-ethylbutyl)cyclohexanecarbonylamino]phenyl] 2,2-dimethylthiopropionate;

S-[2-[1-(2-ethylbutyl)cyclohexanecarbonylamino]phenyl] methoxythioacetate;

S-[2-[1-(2-ethylbutyl)cyclohexanecarbonylamino]phenyl] 2-hydroxy-2-methylthiopropionate;

S-[2-[1-(2-ethylbutyl)cyclohexanecarbonylamino]phenyl] 4-chlorophenoxythioacetate;

S-[2-(1-isobutylcyclohexanecarbonylamino)phenyl] 4-chloro-phenoxythioacetate; and

S-[2-(1-isobutylcyclohexanecarbonylamino)phenyl] 1-acetyl-piperidine-4-thiocarboxylate,

or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

6. A prophylactic or therapeutic agent for hyperlipidemia comprising as an active ingredient the compound as claimed in claim 1, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

7. A prophylactic or therapeutic agent for hyperlipidemia comprising as an active ingredient the compound as claimed in claim 2, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

8. A prophylactic or therapeutic agent for hyperlipidemia comprising as an active ingredient the compound as claimed in claim 3, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

9. A prophylactic or therapeutic agent for hyperlipidemia comprising as an active ingredient the compound as claimed in claim 4, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

10. A prophylactic or therapeutic agent for hyperlipidemia comprising as an active ingredient the compound as claimed in claim 5, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

11. A prophylactic or therapeutic agent for atherosclerosis comprising as an active ingredient the compound as claimed in claim 1, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

12. A prophylactic or therapeutic agent for atherosclerosis comprising as an active ingredient the compound as claimed in claim 2, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

13. A prophylactic or therapeutic agent for atherosclerosis comprising as an active ingredient the compound as claimed in claim 3, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

14. A prophylactic or therapeutic agent for atherosclerosis comprising as an active ingredient the compound as claimed in claim 4, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

15. A prophylactic or therapeutic agent for atherosclerosis comprising as an active ingredient the compound as claimed in claim 5, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

16. A method for inhibition of CETP activity comprising administering to patients the compound as claimed in claim 1, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

17. A method for prevention or therapy of hyperlipidemia comprising administering to patients the compound as claimed in claim 1, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.

18. A method for prevention or therapy of atherosclerosis comprising administering to patients the compound as claimed in claim 1, or a prodrug compound, a pharmaceutically acceptable salt, a hydrate, or a solvate thereof.